Influence of Sociodemographic and Anthropometric Factors on Gallbladder Volume in Pregnancy in a Tertiary Hospital in Nigeria

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Abstract

Objective: The aim of this study is to determine the effect of age, parity, body mass index (BMI) and previous oral contraceptive use on gallbladder volume and ejection fraction in pregnancy, in order to enable obstetricians to identify patients at risk of gallbladder disease in pregnancy.

Methods: This was a prospective cross sectional study involving 190 pregnant women who were evaluated within 32 and 40 weeks of gestation, at the Fetal Assessment Unit of the Department of Radiology, University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria. Patients were scanned with a commercially available *Siemens* Ultrasound scanner using a curvilinear probe and a transducer frequency of 3.5MHz. The fasting gallbladder volume (FGBV) and 30mins postprandial gallbladder volume (PGBV) were calculated using the prolate ellipsoid method. Gallbladder ejection fraction (EF) was determined using the fasting and postprandial gallbladder volumes. A Pro forma was used to document each patient's biodata, medical history as well as somatometric parameters. Ethical approval to conduct the study was obtained from the Ethical Review Committee of the University of Ilorin teaching Hospital, Ilorin, Nigeria.

Results: A total of 190 volunteers were included in the study. BMI showed statistically significant positive, though weak correlations with FGBV (r=0.179, p=0.015) and PGBV (r=0.216, p=0.003) . Maternal age, parity and previous oral contraceptive use did not show any statistically significant correlation with gallbladder parameters.

Conclusion: BMI showed statistically significant, though weak positive correlation with fasting and postprandial gallbladder volumes in pregnancy. The study demonstrated that gallbladder volume in pregnancy may be dependent on BMI. Thus, high BMI may predispose to large gallbladder volume with a resultant increased risk of biliary stasis and gallstone formation in pregnancy. This is relevant for early detection and prevention of gallbladder disease, and follow up including expectant management of subjects that may develop gallbladder disease in pregnancy.

Keywords: Age; Parity; OCP; BMI; Gallbladder Volume; Pregnancy.

Introduction

Gallbladder disease which is relatively common in women and pregnancy has been shown to contribute to the formation of gallstones in females.[1-4] The presence of sludge and gallstones predispose to cholecystitis, gallstone pancreatitis and other morbidities which may require surgical interventions, increase patient stay in hospital, result in frequent hospital visits during pregnancy and trigger preterm deliveries. Maternal mortality, premature delivery and fetal loss may also occur in rare cases.[5-7]

Hormonal changes such as increased serum levels of progesterone occur during pregnancy especially amid the third trimester. These changes cause impaired relaxation of the gallbladder, the resultant effect of which is increased gallbladder volume and stasis of bile which predispose to gallstone formation. [8-11]Other factors that may result in alteration of gallbladder functions during pregnancy are high oestrogen levels and impaired contractility due to cholecystokinin (CCK) secretion.[12,13]

Previous studies have shown that maternal age, parity, body mass index (BMI) and previous oral contraceptive use were implicated in the formation of gallstone in pregnancy. [14-16] This study was carried out using ultrasonography to determine the influence of these risk factors on gallbladder volume in pregnancy in Ilorin, Nigeria. Ultrasonography; non-ionizing and non-invasive, helps in early detection of large gallbladder volume and poor contractility and hence, also help to identify at-high risk patients. [17-20] This is relevant for early commencement of preventive measures, such as dietary modification, weight reduction and physical activity, thereby, preventing gallstone formation[21]. Furthermore, for patients who may develop gallbladder disease in pregnancy, prompt management of such patients by the obstetrician can prevent complications of gallbladder disease to the fetus and mother. Management options may include discontinuation of oral intake, intravenous fluid replacement, analgesia and antibiotics treatment or surgical interventions (cholecystectomy) [21-23]

Methods

This study was a prospective cross sectional study in design .and was carried out in the Fetal Assessment Unit (FAU) of the Department of Radiology, University of Ilorin Teaching Hospital (UITH). A total of 190 pregnant women between 32-40weeks of gestation referred for routine obstetric scan from the Department of Obstetrics and Gynaecology, UITH, were recruited. Gestational age was evaluated using last menstrual period (LMP) and/ or early trimester Ultrasound scan.

The study procedure and benefits were thoroughly explained to patients during antenatal visits. They were told that they will observe at least 12hours overnight fast prior to the day of the study (to ensure satisfactory gallbladder distension and to reduce the amount of gastric and intestinal gas), and that two upper abdominal ultrasound scan will be carried out on them before and after ingesting 2sachets of *Three Crowns Filled* Evaporated Milk. Consenting patients were consecutively recruited until the desired sample size was obtained.

Sample size was determined using Leslie Fisher's formula which is stated as follows

$$\text{Sample size (n)} = z^2pq/d^2$$

Where z= standard normal deviation usually set at 1.96, which correspond to 95% confidence interval.

P= prevalence of gallstone in pregnancy in a city in Nigeria (2.9%) [2]

q= 1.0-p

d= the degree of accuracy required usually set at 0.05.

n= 1.96x 1.96 x 0.029 x 0.971/0.05x 0.05 = 43

Sample size was increased to 190 to improve the validity of the study. Patients who had comorbid conditions such as diabetes mellitus, sickle cell anaemia, hypertension and pre-eclampsia including patients with other systemic illness such as gastrointestinal, gallbladder, liver or other endocrine diseases were excluded from the study. Patients taking medications known to affect gallbladder emptying such as calcium channel blockers, opioids, anticholinergics, progestogens and oestrogens, post-cholecystectomy patients, patients who have allergy to liquid evaporated milk and patients with multiple pregnancies were also excluded from the study.

A self-designed Pro forma was used to record biodata, obstetric history, medical history, fasting and postprandial gallbladder volumes as well as ejection fraction. All booking investigations such as haemoglobin genotype (to rule out sickle cell anaemia), urinalysis(to rule out pre-eclamsia), blood sugar estimation (for patients at risk such as patients family history of diabetics and obese patients) were reviewed.

Weight and height were measured using standard weighing scale and Stadiometer respectively. BMI was calculated as weight (kg)/ height(m)^2.

A *Siemens* Sonoline SI-400 Ultrasound scanner with a 3.5MHz curvilinear probe and acoustic coupling gel were used for the study. Patients were positioned supine on an examination couch and the abdomen exposed down to the pubic line. After applying coupling gel to the skin, a brief obstetric scan was done to ascertain the gestational age. This was determined using a combination of multiple biometric parameters{ biparietal diameter (BPD), femur length (FL) and abdominal circumference (AC)}, and compared with published Western Nomogram (Hadlock's) for each parameter.[24]

Compliance with fasting was ascertained by scanning the stomach and duodenal regions for food residue or fluid. Two serial right upper quadrant scans were subsequently done to assess the maternal gallbladder: before drinking 120ml (2sachets) of *Three Crowns Filled* Evaporated Milk (produced by FrieslandCampina WAMCO Nigeria PLC®, which contains 10.2g of fat, 8.9g of protein and 14.3g of carbohydrate) and thirty minutes postprandial respectively.

The length of the gallbladder was measured on breath holding using the maximum longitudinal dimension, either in supine or right anterior oblique position (Fig 1a). The probe was rotated through 90º to obtain the maximal transverse dimensions i.e., the width and height, with the calipers crossing each other at 90º (Fig1b). Inner to outer wall dimensions were used for all measurements. Measurements were taken thrice and the average for each recorded. Measurements of gallbladder dimensions were repeated 30minutes postprandial.

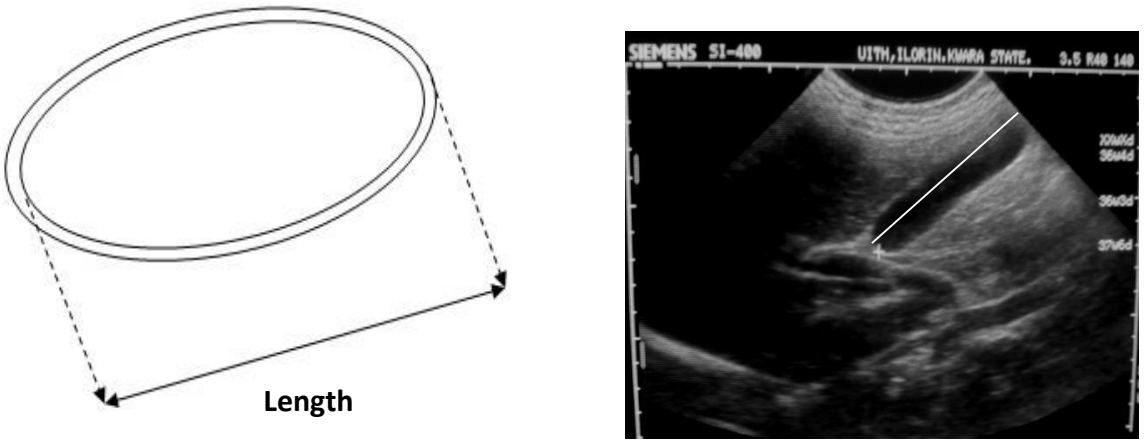

Figure 1a: Line diagram and US image of Longitudinal view of Gallbladder showing.

length measurements

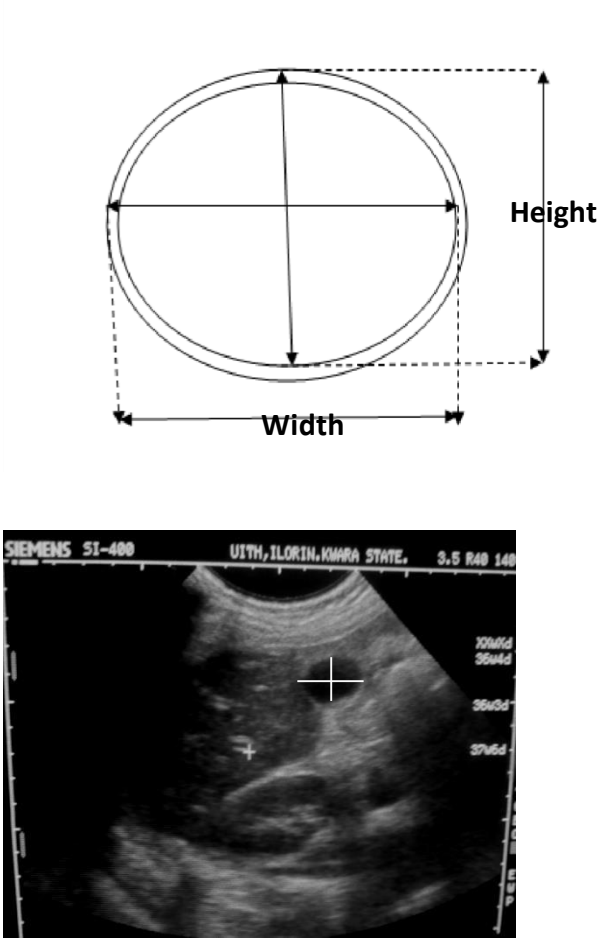

Figure 1b: Line diagram and US image of transverse view of Gallbladder showing width and height measurements.

Gallbladder volumes (fasting and postprandial) were subsequently obtained using the ellipsoid method (volume =length x width x height x 0,523). [25] Ejection at 30minutes was calculated by the following equation.

Ejection fraction (EF) [26] = (FGBV-PGBV)/FGBV X 100. Where FGBV is the fasting gallbladder volume and PGBV is the 30minutes postprandial gallbladder volume.

Ethical approval to conduct the study was obtained from the Ethical Review Committee of the University of Ilorin teaching Hospital, Ilorin, Nigeria.

Data analysis

The data was entered and analyzed using the Statistical Package for Social Sciences version 21. (SPSS Inc. Chicago, IL, USA). Gallbladder volume and ejection fraction was the dependent variable with parity, maternal age, BMI and previous oral contraceptive use as independent variables respectively. The strength and the direction of the relationship between the gall bladder volume and ejection fraction; parity and BMI were analyzed using Pearson's correlation coefficient. Spearman's correlation coefficient was used for its relationship with age, while its relationship with previous oral contraceptive use was analysed using Independent samples T test. Probability (*p*) values < 0.05 was considered statistically significant.

Results

A total number of 190 participants were evaluated. Participants age range from 16- 45years with a mean (±SD) of 29.53 ± 6.15 years.(table 1). Most of the participants (31%) were primiparous(parity 1). The mean(±SD) gestational age was 35.45±2.28 weeks (figure 3). Fewer respondents (31.8%) had histories of previous OCP use. A mean (±SD) BMI of 26.87±5.48 was obtained. The mean(±SD) FGBV was 46.76±21.28ml, while mean(±SD) PGBV was 21.14±13.26. A mean (±SD) ejection fraction of 49.81±65.76% was obtained.

Table 1: Age of study participants.

Variable	**Frequency**	**Percent**
Age group (years)		
16-20	8	4.2
21-25	38	20.0
26-30	75	39.5
31-35	36	18.9
36-40	22	11.6
41-45	11	5.8

Mean age of participant: 29.53±6.15 years

Maternal age showed weak positive correlations with FGBV (r=0.077) and PGBV (r=0.068). A weak negative correlation was noted with EF (r= -0.029). However, there was no statistically significant relationship between previous maternal age and gallbladder parameters (p= 0.305, 0.369, 0.699 respectively) as shown in table 2.

Table 2: Correlation of Parity, Maternal age and BMI with Gallbladder parameters.

	Fasting gallbladder		**30 minutes postprandial**		**Ejection fraction volume gallbladder**	
Variables	R	***p*-value**	R	***p*-value**	R	***p*-value**
Maternal age	0.077*	0.305	0.068*	0.369	-0.029*	0.699
Parity	0.102	0.166	0.034	0.649	0.014	0.852
BMI	0.179	0.015	0.216	0.003	0.520	0.478

*R: Pearson's correlation coefficient; *spearman's correlation coefficient.*

Parity showed weak positive correlations with FGBV (r=0.102), PGBV (r=0.034) and EF (r=0.014) and that were not statistically significant (p= 0.166, 0.649, 0.852 respectively) (table 2). BMI showed statistically significant positive, though weak correlations with FGBV (r=0.179, p=0.015) and PGBV(r=0.216, p=0.003) . A positive correlation (r= 0.520) was also observed with EF but was not statistically significant (p=0.478) (table 2). Previous oral contraceptive use showed a weak positive association with FGBV(t= 0.067), but a strong positive association was observed with PGBV(t= 0.981) and EF (t=0.655). However, there was no statistically significant relationship between previous OCP use and the gallbladder parameters (p= 0.967, 0.328, 0.173) as shown in table 3.

Table 3: Oral contraceptive use and Gallbladder parameters.

Variable	**Yes (Mean ± SD)**	**No (Mean ± SD)**	**T**	***p*-value**
Fasting gall bladder volume (ml)	47.18 ±19.62	46.74±21.43	0.067	0.967
30 minutes postprandial gallbladder volume (ml)	17.34±7.79	21.38±13.49	0.981	0.328
Ejection fraction (%)	62.43±13.51	49.0367.63	0.655	0.513

T: Independent samples T test;

Discussion

Prompt identification of possible sociodemographic and anthropometric factors that may influence gallbladder volumes in pregnancy is vital in order to prevent formation of gallbladder disease in pregnancy, and also for early management of patients who may develop gallbladder disease. There was no statistically significant correlation between maternal age and gallbladder volumes. This was contrary to a previous study in Italy by Palasciano *et al* on healthy adults, where gallbladder volume was shown to correlate positively with age. [27] This was also at variance with a related previous study by Brian and colleagues in Nairobi, Kenya. [28] Agarwai *et al* in a similar study in diabetics observed that the positive correlation of age and gallbladder volume was as a result of spontaneous autonomic denervation of gallbladder with aging, leading hypomotility, bile stasis and increased

gallbladder volume.[29] However, differences in subject population may be the reason for the contrary findings in this study. Furthermore, there was also no significant correlation between maternal age and gallbladder ejection fraction, similar to findings by Ugwu *et al*.[30] This finding also agrees with those of Wedman and colleagues.[31]

Higher parity has been shown to be associated with increased lifetime exposure to oestrogen which alter composition of bile and impair biliary motility (or ejection fraction) with resultant increased gallbladder volume and gallstone formation.[32] However, this study does not show any statistically significant correlation between parity and gallbladder volumes and ejection. This also agrees with a study on gallbladder dysmotility in pregnancy by Ayse *et al.*[33] Nahum *et al* in a similar study in pregnant women was only able to demonstrate significant correlation between parity and gallbladder ejection fraction[21]. Agarwa and colleagues showed significant correlation between parity and gallbladder volume. Nonetheless, their study was done on diabetic patients.[29] Most of the participants in this study were primiparous and this may be the reason for the contrary findings in this study.

BMI showed statistically significant but weak positive correlation with gallbladder volumes in this study. Though, a strong relationship between gallbladder volume and BMI was obtained by Sari *et al* in their studies on gallbladder volume in obese women in Turkey.[34] Findings similar to that obtained by Sari and colleagues were observed in a similar study on healthy adults in Kano, Nigeria.[35] Then again, Adeyeku and co-workers in Benin, Nigeria did not show any correlation between BMI and gallbladder volume.[36] Other researchers have demonstrated greater gallbladder volumes with increased BMI. It has been documented that higher BMI is associated with excessive body visceral fat and insulin resistance which may predispose to gallbladder motility defect. Hence, large gallbladder volumes, gallbladder stasis and gallstone formation.[37] In addition, autonomic neuropathy or reduced gallbladder sensitivity to cholecystokinin may also be contributory.[38] The relatively weak positive but statistically significant correlation between gallbladder volume and BMI in this study may be due to dietary factors or racial differences. Nevertheless, no statistically significant relationship between BMI and ejection fraction was obtained in this study. This is in consonance with previous study by Bradford *et al*,[39]but at variance with results obtained in the study by Ugwu *et al.*[30] Leonardo and colleagues[40] observed gallbladder contractility(or ejection fraction) in obese patients than controls, and similar results were obtained by Fraqueli et al.[38]The contrary findings in this study may be due to difference in study population or racial differences

Previous studies have shown that oestrogen and progesterone, both active components of oral contraceptive pills(OCP) cause decreased gall bladder contractility which impedes biliary flow, hence increased gallbladder volume and resultant gallstone formation.[41,42] However, this study showed no significant association between previous oral contraceptive use, and gallbladder volume and contractility (ejection fraction). This is in consonance with a related study by Braverman and colleagues.[43] Pansini *et al* also in a similar study, but in healthy non pregnant women showed no significant difference in gallbladder volume between previous users and non-users of OCP.[44] Few respondents reported positive history of previous OCP use, and this may be responsible for the non-association between previous OCP use, gallbladder volume and contractility.

Limitation of Study

The response rate regarding the use of OCP was poor so results must be interpreted with caution and conclusion cannot be drawn

Conclusion

Among the sociodemographic and anthropometric factors, only BMI showed statistically significant but weak positive correlation with gallbladder volume in pregnancy. Thus, the study demonstrated that gallbladder volume in pregnancy may be dependent on BMI. Consequently, high BMI may predispose to large gallbladder volume with a resultant increased risk of biliary stasis and gallstone formation in pregnancy During obstetric ultrasound examination, maternal gallbladder should be evaluated quickly, especially in patients with risk factors such as high BMI. This is relevant for early commencement of preventive measures such as dietary modifications, weight reduction and physical activity in order to prevent gallbladder disease in pregnancy. This is also necessary for follow up and expectant management of patients that may develop gallbladder disease in pregnancy. Management options may include conservative (discontinuation of oral intake, intravenous fluid replacement, analgesia and antibiotics treatment) or surgical (cholecystectomy) approach. However, there is paucity of data on the influence of sociodemographic and anthropometric factors on gallbladder volume in pregnancy. There is therefore the need for further multicentre research so as to obtain data that may be used to compare with results of this study and thus generate a more generally acceptable reference data.

Disclosure on Conflict of Interest and Financial/Material Support

There is no conflict of interest and the authors had no source of financial or material support and assistance

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